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STANDARDS IN PHARMACEUTICAL EDUCATION.1

BY HENRY KRAEMER.

If we consider the present awakening in pharmacy, it may seem to some that we are making very rapid strides, but as a matter of fact the progress of pharmaceutical education in this country has been comparatively slow. The history of pharmacy in this country may be divided into three periods: (1) The pioneer period during the sixteenth century, when there were no physicians, and the general storekeeper who sold dry goods, groceries, books and paints, also sold medicines and prescribed them; (2) the colonial period during the seventeenth and eighteenth centuries, when educated physicians from abroad emigrated to the colonies and prescribed as well as dispensed medicines; (3) the college period, or the period of organization and development, during the nineteenth century, when pharmacy became a distinct profession and business, and colleges of pharmacy were established, these numbering nearly 100 at the present time. We are now entering, after nearly a century, upon the fourth period, namely, that of standards in education, and we are endeavoring to fix the position of pharmacy among the other professions.

The problem of pharmaceutical education involves two phases, namely (1) that of the natural ability and preliminary qualifications of the applicants for entrance to the colleges and schools of pharmacy, and (2) that of the character and kind of instruction that shall be given by a recognized teaching institution in pharmacy.

¹ Read before the Philadelphia Branch of the American Pharmaceutical Association, February 5, 1907.

Not only are these two classes of standards being considered by the teaching bodies themselves, but also by the boards of pharmacy. and with the enactment of laws in various States it will now be possible for more or less concerted action to be taken throughout the United States.

PRELIMINARY REQUIREMENTS.

Our system of popular education is the boast of our country, and well may it be, for it has been making steady advances during all the years of our national existence. At the present time the facilities for instruction and the opportunities for obtaining a good general education are so ample that it seems hardly credible that any one who is desirous of obtaining an education should fail in the attempt.

It follows logically that as the standard of general education is advanced, the standards in colleges, technical schools and universities will also be advanced, and thus we find to-day that the majority of these institutions are not only constantly improving their curricula but they are seeing to it that those who go to them for instruction are qualified to pursue the prescribed line of studies. The only wonder is that the entrance standards in some of the professional schools have not been advanced more rapidly than they have, for in no other way have they been more handicapped than in this.

It is true there may be some parts of our country where the opportunities for obtaining an education are more or less limited, but this is no argument why those in the vanguard should stop in their course and wait for the center of population to shift a few hundred miles. We know that in Alaska and the Philippines the means for education are not so ample as they are with us, but we are not thinking of stopping to wait for those countries. On the contrary they desire us to go ahead and they will follow as rapidly as possible. And so if the youths of the country districts of Iowa, or Kansas, or Missouri have not, as is claimed by some, the opportunity for obtaining a high-school education, is that any reason why those in Ohio, or Michigan, or Pennsylvania should be excused for neglecting theirs? No, this is not the way of progress.

If there are any two professions or callings where the unfit should be culled out more than in others, it is in those of medicine and pharmacy. These are the professions calling for the highest type of manhood, and at the same time special educational equipment and intellectual acumen. Being largely answerable to himself in the conduct of his business, it is plain that the pharmacist must be of a high moral type, and if he is of the type that he should be to assume such a responsible calling, he will first see to it that his general education warrants him in undertaking its pursuit. But if there are those who have not the moral sense to conscientiously qualify themselves by obtaining the necessary preliminary education, then the teaching bodies should exercise their power to eliminate them. Here is where the highest obligation of the schools and colleges of pharmacy rests, and here is where the supreme test of their sense of their obligation to the public comes in.

Certainly those applicants for entrance who have had opportunities for obtaining an education and have been so indifferent as not to improve them, can hardly be considered fit candidates for the practice of pharmacy. Entrance to a college presupposes a good general education; the studies to be mastered require it, and to admit the unqualified reacts on all those engaged in the practice of pharmacy and in the teaching of pharmacy. It also does harm to those who are still in the public schools, for instead of finishing their courses they discontinue their studies knowing that they can fit themselves by short cuts. It lowers the standard of the schools of pharmacy and so tends to keep away those who are qualified to pursue the work. In short, it lowers the tone of pharmacy at every point. And who can say that it does not eventually make an impression on the general public and influence them in withholding their support, both moral and financial?

I know of a young man who desired to study law, but who had not gone further than the grammar school. When he came to inquire about the terms of admission to the bar, he found that graduation from a high school was required. He then decided to enter school again and go through the high school. Can any ore doubt the advantage of such a course to this young man or to the profession of law in requiring him to complete his preliminary education?

There are those who incline to take pity on those applicants in pharmacy who have not the desired amount of preliminary education and who argue that they should be given a chance. But this is a false kind of charity; if the applicants are sincere and have natural ability, they should be advised to go back to school, but if they belong to the shiftless class, they should above all things not be allowed to ally themselves with pharmacy. No, this is not the place for the exercise of charity, particularly when we think of our obligations to the great public who have so long and so implicitly trusted us.

COLLEGE COURSES.

Having once eliminated the unfit, the next highest duty of the colleges of pharmacy is to qualify their students for the work that they may be called upon to do. This may seem like a very trite saying to some of you, and yet I feel warranted in its utterance. We have reached a crisis in pharmaceutical history, and if the pharmacist is to continue a separate and independent existence it must be on the basis of his scientific attainments. The pharmacist has felt his hampered position for some time, but now that the Pure Food and Drugs Act has become effective, we are face to face with the issue. With the United States Pharmacopæia and the National Formulary as the legal standards he will now be held responsible for the identity and quality of the drugs which he sells. The question then is, will he assume this responsibility, and pronounce finally on the quality and efficiency of the drugs and medicines which he dispenses, or will he shift this responsibility whenever possible? If he adopts the latter course, then will he lose in importance and standing to that extent.

By the adoption of the Pure Food and Drugs Act both the responsibility and the obligation of the pharmacist are increased and added importance must attach to his position. He should take as much pride in his ability to pronounce upon the quality of an article guaranteed by the manufacturer, or in making a preparation which he himself guarantees, as he has heretofore taken in his ability to decide upon the compatibility, or to question the dosage, of a prescription. He must stand between the manufacturer and the physician as he has stood between the physician and the public. Too much care cannot be exercised in this direction, for the manufacturer's guarantee may in some instances prove to be only a label.

To do work of this kind means that the pharmacist shall be a master of the Pharmacopæia, that he shall be able to identify any substance in the Pharmacopæia, carry out any of the tests, and make any of the preparations in the Pharmacopæia and National Formulary, processes for which are given. The least, then, that the colleges of pharmacy can do is to prepare their students to employ the Pharmacopæia and the National Formulary as working guides.

EXAMINATIONS BY BOARDS OF PHARMACY.

With the proper preliminary requirements established, and without entering at this time into a discussion of the question as to the number of hours required for the work that should be done, believing as I do that the colleges and schools belonging to the Conference of Teaching Faculties will be able to decide this problem, I may say that no discussion of the educational problem is complete at this time without reference to the nature of the examinations of the Boards of Pharmacy. In years gone by these examinations have been largely theoretical, and hence were not so valuable as they might have been in testing the fitness of a candidate. Happily, there is beginning to be an improvement in this direction and the examinations are becoming more practical. To my way of thinking the aim of the boards of pharmacy should be to determine what a candidate can do. The theory has been given to him in college, and the final test should be to determine whether he has a working knowledge of the materials which he handles. Instead of asking him what are the elementary forms of matter, or what is a water-bath, or to give the family name of a plant yielding a drug, it would be better to give him some drug or chemical to identify, to carry out the tests for purity according to the Pharmacopæia and to make a preparation.

The boards of pharmacy have a very important work to perform in determining the fitness of candidates and in determining whether the colleges are faithfully carrying on their work. As matters are now constituted they are the final arbiters and should be fully cognizant of the great trust which they hold. It should no longer be possible for the unqualified or incompetent to enter college, spend two or three years at college and be given a degree and finally pass a State Board as a registered pharmacist.

THE DUTY OF PHARMACISTS.

Pharmacists themselves also have a very important part to perform in raising pharmacy to the plane that it must occupy to maintain its separate existence. In the first place they should not admit into apprenticeship young men who are deficient in preliminary education, for quite naturally they hope sooner or later to enter the schools of pharmacy. Indeed to admit such as these into apprenticeship is not only an injustice to them but also to the colleges of pharmacy, and this may be considered as one of the fundamental tests as to whether the pharmacist has the true interests of his calling at heart. Pharmacists can at this point be of real service to these young men by encouraging them and advising them to continue their education in the public schools or to acquire it in some other way.

The second duty of the pharmacist is to endeavor to conduct his business in such a manner that the educated young men will be attracted to it (for undoubtedly there is no more interesting work than that connected with the profession of pharmacy), and find something to repay them for their pains, and to appeal to their aspirations as professional men.

The third duty of the pharmacist is to the physician. If the physician is willing to rely upon the pharmacist and to help him in maintaining and re-establishing the profession of pharmacy by prescribing only the preparations and medicines in the Pharmacopæia and National Formulary, and the new and non-official remedies approved by the Council on Pharmacy and Chemistry of the American Medical Association, then should the pharmacist aim to eliminate as rapidly as possible patent medicines, nostrums and sundry articles not used as medicines, or as aids to the sick, or even as toilet preparations, and prepare to give his undivided attention to his profession, which alone by training, education and experience he is qualified to conduct.

In briefly summing up my remarks I may say that I have endeavored to emphasize the essential principles which we must bear in mind.

- (1) A good preliminary education is essential to an apprentice and student of pharmacy.
- (2) The least that a college or school of pharmacy should do is to send forth graduates that are masters of every detail of the U. S. Pharmacopæia and the National Formulary.
 - (3) It is the duty of the Board of Pharmacy to determine what

applicants for the certificate of Registered Pharmacist can do rather than what they are able to memorize.

(4) That pharmacists themselves must share in the work of elevating the standards of pharmacy.

If we are clear on these principles, sincere in our professions and earnest in our endeavors, the details can easily be worked out.

THE FOOD AND DRUGS ACT IN ITS RELATION TO PUBLIC HEALTH.

BY CHARLES H. LAWALL.

The responsibility of the pharmacist in his attitude toward fraud and quackery was never more important than it is at the present time, and there should be no reluctance on the part of the members of the profession to serve the public in the capacity of disseminators of information concerning this important subject which is everywhere under discussion, the Food and Drugs Act.

In the United States the actual control of the quality of food and drugs within any given State is a power of the State and not of the federal authority, and owing to the previous absence of legislation controlling interstate commerce the authorities within the individual States (usually the Dairy and Food Commissioner) were confined to the boundaries of these States in bringing prosecutions. In order to control the sale of products made outside of the State and shipped into it, the seller, often an innocent victim, had to be proceeded against, and the manufacturer, the real offender, was secure from any punishment as long as he remained without the State.

This condition of affairs, of course, worked hardship upon persons who were not morally responsible, who were made defendants in criminal prosecutions and were compelled to resort to the civil courts for redress, which was usually inadequate.

On June 30, 1906, by the passage of the act known as the Food and Drugs Act, which went into effect legally on January 1, 1907, this condition of affairs was changed, and every article of interstate commerce is now subject to the act, the rules and regulations of which have occasioned much serious thought among the large class of manufacturers of products which come within its scope.

The underlying principles of the act, and the rules and regulations

which have been drafted for its enforcement, are not obscure. They are based upon common honesty. That is, no hardship is worked upon persons who sell their products for what they are, without any misrepresentation. This at first glance would not seem to be a harsh requirement, but when we go into the subject a little more fully we are confronted with the fact that the present era of advertising has developed a carelessness of statement to say nothing of numerous instances of wilful misrepresentation suggesting that the allegation of P. T. Barnum that the American people like to be humbugged, was never more true than at the present time.

Academic questions as to the harmfulness of certain preservatives or colors, or substitutes for this or that well-known foodstuff, do not enter into the question at all. The phrase "caveat emptor," let the buyer beware, is not applicable to foodstuffs, for the buyer as a rule is not capable of judging as to the presence or absence of certain constituents which may or may not be harmful according to the idiosyncrasy of the consumer.

For example, fifty or seventy-five years ago the commonly used chemical preservatives, salicylic and benzoic acids and saccharin were unknown and when they were resorted to by manufacturers of foodstuffs it was done secretly and without notice to the consumer. While the presence of a small amount of any one of these substances might not occasion any disturbance in a normal individual there are many instances in which even small amounts are absolutely contraindicated. Under commercial conditions existing previous to the passage of the act mentioned the buyer never could tell just what was contained in a package, which might be marked absolutely pure and be decorated with representations of dozens of medals and prize awards, often based upon superficial judgment of the products so honored.

The misbranding clause is Section 8 of the law and reads as follows:

"That the term 'misbranded' as used herein shall apply to all drugs or articles of food, or articles which enter into the composition of food, the package or label of which shall bear any statement, design or device regarding such article, or the ingredients or substances contained therein, which shall be false or misleading in any particular and to any food or drug product which is falsely branded as to the State, territory or country in which it is manufactured or produced."

Since the act has become effective the products of certain large packing houses, which were formerly called potted ham or potted tongue are now labeled "potted meat, ham-flavor" and "potted meat, tongue-flavor." The substance has not been changed. It is simply designated by its right name and all the claims for purity made by these firms in the past are now to be judged by the actions of these same firms when under compulsion and in fear of the law.

Several years ago a well-known Philadelphian became sponsor for a brand of coffee which was advertised and sold under the caption of "tannin-free coffee." This purported to be coffee from which the poisonous (?) tannic acid had been removed. Investigation showed it to be coffee from which a chaff-like substance lying between the segments of the bean had been removed by mechanical means, and, as this chaff-like substance was found to contain less tannic acid than the original coffee, and, as the statement as to the tannic acid being poisonous was equally unwarranted, it was one of the most reprehensible of the class of what would now be termed misbranded substances.

As a matter of fact the tannic acid in coffee is in such intimate combination with the caffeine and other valuable constituents of the bean that it would be absolutely impossible to remove it without destroying the properties of the coffee so that it would be unrecognizable.

The ultimate fate of this article, which perished along with several associated ventures, did not prove a deterrent to another and still more glaring fraud of a similar character which has been advertised during the past year, i. e. a brand of coffee called "Digesto Coffee" which claims to be as harmless as the well-known cereal substitutes for this agreeable beverage by virtue of the fact that the poisonous (?) caffeine and poisonous (?) tannic acid have both been removed. I need scarcely say that such claims are without the slightest foundation in fact, and an analysis recently made by me of the contents of a package of the article showed a slightly higher percentage of caffeine than the average in coffee, and no perceptible diminution in the amount of tannic acid.

I refer to both of these instances specifically, as under all previous laws it was impossible to proceed against either of these firms, while under the new law they are both amenable to the section on misbranding.

As regards the subject of drugs, the work of Samuel Hopkins Adams in Collier's Magazine, together with the assistance of Mr. Bok in the Ladies' Home Journal, is too well known to require repetition, and yet I fear that the force of these arguments is lost upon many persons who look upon them as the fulminations of yellow journalism. Nothing could be further from the truth. The half has never been told and the real truth will probably never be known by the public concerning the numerous changes which have been made in many well-known preparations which must now declare the presence of certain constituents which are enumerated in the body of the law. Among the better known of these substances may be mentioned alcohol, morphine, opium, cocaine, chloroform, chloral hydrate, cannabis indica and acetanilide.

Many proprietors of nostrums which have been entirely dependent upon their alcoholic strength for their medicinal and remedial effect, have changed the formulas so as to be less liable to criticism, still retaining enough of the original features, however, to make them objectionable to those who see through the subterfuge.

The number of persons in the community who are really able to judge such preparations is wofully small and it will require a constant campaign of education for many years to bring the every-day consumer of preparations of this class to a sense of his personal responsibility in such matters.

Even the medical profession has suffered by this gigantic bunco game.

Antikamnia, a proprietary preparation which was advertised for years under the claim that it was a definite synthetic compound, in spite of the fact that every one who knew anything about organic chemistry knew better, has at last been publicly unmasked as a mixture of acetanilide, caffeine and sodium bicarbonate; and in refuge from the necessity of declaring the amount of acetanilde upon the label, the firm which makes it has changed the formula so as to substitute phenacetine for acetanilide, and yet the same unwarranted and extravagant claims are made for the preparation that were made before, with no notice to the medical profession that a radical change has been made in its composition, and entirely ignoring the stultification of the former claims as a definite uniform chemical compound.

Other instances might be cited, but enough has been said, I think,

to show you that the effect of the law is being felt by those who have made themselves amenable to it.

One important feature must be remembered. It is this: On every package of foodstuff or drug put up under the new law, the words "Guaranteed under the U. S. Food and Drugs Act, June 30, 1906, Serial No. ——" appears. This is being used in such a way as to make it appear that the Government in some unknown way stands sponsor for the quality of the substance, when in truth it is but a compliance with that part of the Act, Sec. 9, which says:—

"No dealer shall be prosecuted under the provisions of this act when he can establish a guarantee signed by the wholesaler, jobber, manufacturer, or other party residing in the United States, from whom he purchases such article, to the effect that the same is not adulterated or misbranded within the meaning of this act designating it."

Thus it will be seen that the guaranty means nothing more than the word of the manufacturer that he will be responsible in case of prosecution, and I fear that not a few of the guarantees at present published are given without due regard to facts, in the hope that the Department of Agriculture, with the tremendous task confronting it of putting the rules and regulations into practice, may be a long while reaching some of these articles.

Meanwhile many persons will be deluded into purchasing such articles in the belief that the phrase referred to is evidence that the Government is responsible for the claims made, when in point of fact nothing of the kind is meant.

An instance recently coming to my attention, presumably of this kind, is that of an article which is being advertised in the prominent daily newspapers in the form of reading notices (a most reprehensible form of advertising) as a remedy for consumption and bronchial affections. An examination of the substance shows it to be a fictitious product containing oil of turpentine, gum turpentine, with evident traces of copaiba and sandalwood. It bears a label which indicates a somewhat mixed origin, as two widely differing plants of the pine family are included in the botanical name which is given for it.

In the regulation of the narcotic drugs, such as opium and its derivatives, morphine, cocaine, etc., a wonderful step has been taken. If the public could realize the harm that has been done to persons

who have unconsciously formed drug habits by taking proprietary catarrh cures there would be universal amazement at the depths of degradation to which a manufacturer will lower himself in order to increase the profit on an article by stimulating an increase in its sale. Instances have come before the authorities at Washington in which manufacturers have frankly admitted that they had added morphine or cocaine to their nostrums in order that their continued use might be assured.

There is much work still to be done in the near future in connection with the enforcement of the act to render its provisions effective, but I believe that I have given enough examples from the hundreds which I have at my disposal to indicate that the ultimate effect of the Food and Drugs Act, if it be wisely enforced, as is expected, will be very material in benefiting the health of the community at large.

PROPRIETARY PREPARATIONS APPROVED BY COUNCIL ON PHARMACY AND CHEMISTRY.

ARISTOCHIN.

Aristochin.—CO $(C_{20}H_{25}N_2O_2)_2$ — $C_{41}H_{46}N_4O_5$, the neutral carbonic ester of quinine.

Actions and Uses.—The same as those of quinine, but, since it is only slowly acted on by acids, it is said not to produce disturbance of the stomach and to be notably free from tendency to production of cinchonism. Dosage.—The same as that of quinine, in powder, mixed with milk sugar, dry on the tongue or suspended in liquids. Manufactured by Farbenfabriken, vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color & Chemical Co., New York).

ARISTOL.

A name applied to Thymolis iodidum, U.S. P. Manufactured by Farbenfabriken, vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color & Chemical Co., New York).

ASPIRIN.

Aspirin $C_6H_4O(CH_3CO)$ COOH 1: $2 = C_9H_8O_4$, the acetyl derivative of salicylic acid.

Actions and Uses.—It acts like salicylic acid, over which it possesses the advantage of producing less of the undesired local and systemic side effects, on account of the slow liberation of the salicylic acid. It passes the stomach unchanged, the decomposition beginning in the intestine. Dosage.—0.3 to I gramme (5 to 15 grains) in capsules or wafers, or dissolved in sweetened water or dry on the tongue, followed by a swallow of water. The powder should be dispensed in waxed paper. Manufactured by Farbenfabriken, vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color & Chemical Co., New York).

BENZOSOL.

Benzosol, $C_6H_4(OCH_3)$ $C_6H_5COO) = C_{14}H_{12}O_3$, a crystalline compound of guaiacol in which the hydrogen of the hydroxyl is replaced by benzoyl.

Actions and Uses.—Benzosol is decomposed slowly in the intestinal tract into guaiacol and benzoic acid which exert their proper actions. The liberated constituents are absorbed and excreted in the urine. It is not irritating. Its uses are analogous to those of creosote and of benzoic acid. It is recommended in incipient pulmonary tuberculosis, as an intestinal antiseptic in fermentation, diarrhea, typhoid fever, diabetes mellitus and as a urinary disinfectant in cystitis, etc. Dosage.—0 2 to 0 6 gramme (3 to 10 grains), in powder, capsule, pill, or suspended in liquids or as an emulsion. Manufactured by Farbwerke, vorm. Meister, Lucius & Bruening, Hoechst a. M. (Victor Koechl & Co., New York).

BETA-EUCAINE HYDROCHLORIDE,

Beta-eucaine hydrochloride, $C_5H_7N(CH_3)_3$ (C_6H_5COO)·HCl, the hydrochloride of 2,6,6 trimethyl-4-benzoyl-hydroxypiperidine.

Actions and Uses.—Beta-eucaine hydrochloride is a local anesthetic like cocaine, but weaker and devoid of the stimulating properties of the latter. It does not dilate the pupil, nor does it contract the blood-vessels as does cocaine. It has the advantage of stability even on prolonged boiling. It may be used in all cases in which cocaine is indicated as a local anesthetic, especially in ophthalmology. Dosage.—It may be applied in a 2 to 3 per cent. solution to the eye, 5 to 10 per cent. for nose and throat, and 5 to 10 per cent. for ointment for hemorrhoids. Manufactured by Chemische Fabrik auf Actien, vorm. E. Schering, Berlin (Schering & Glatz, New York).

BETA-NAPHTHOL BENZOATE.

Beta-naphthol benzoate, C_6H_5 ·COO· $C_{10}H_7 = C_{17}H_{12}O_2$, the benzoic ester of β -naphthol.

Actions and Uses.—Beta-naphthol benzoate is split up into its constituents on reaching the intestinal tract and acts as an antiseptic. It is said to be diuretic. It is used internally as an intestinal antiseptic in diarrhea and typhoid fever. Externally it has been recommended as a parasiticide in the form of 3 to 10 per cent. ointment, and has been used in psoriasis, eczema, scabies, etc. Dosage.

—0.2 to 0.5 gramme (3 to 8 grains); maximum dose, single, I gramme (15 grains), daily 4 grammes (60 grains). Manufactured by Fabrik von Heyden, Radebeul near Dresden (Merck & Co., New York).

BETOL.

Betol, C_6H_4 ·OH·COO $(C_{40}H_7) = C_{17}H_{12}O_3$, the salicylic ester of β -naphtol.

Actions and Uses.—Betol is not affected in the stomach, but is split up in its original components when it reaches the intestinal tract by the pancreatic juice and intestinal secretions. It is believed to act as an intestinal antiseptic and, being excreted in the urine, to act in a similar way in the bladder. It has the anti-rheumatic properties of salicylic acid. It is recommended for intestinal fermentations, catarrh of the bladder, particularly in gonorrheal cystitis, for rheumatism, etc. Dosage.—0.3 to 0.5 gramme (4 to 8 grains) in cachets, milk or emulsion. Manufactured by the Heyden Chemical Works, New York.

BISMAL.

Bismal, 4 $(C_{15}H_{12}O_{10})\cdot 3Bi(OH)_8 = Bi_3C_{60}H_{57}O_{49}$, a compound of bismuth hydroxide and methylendigallic acid.

Actions and Uses.—Bismal is an astringent and is recommended for the treatment of chronic diarrhea. Dosage.—0·12 to 0·3 gramme (2 to 5 grains) in cachets or powder. Manufactured by E. Merck, Darmstadt. (Merck & Co., New York.)

BOROCHLORETONE.

A mixture of 1 part chloretone with 3 parts boric acid. Actions and Uses.—An antiseptic and anesthetic, used externally as a surgical dressing powder. Prepared by Parke, Davis & Co., Detroit, Mich.

. BROMETONE.

Brometone, 1,1,1-tribrom 2 - methyl - propan 2-ol, $CBr_3 \cdot C(OH)$ (CH_3) $CH_3 = C_4H_7OBr_3$, produced by the reaction of acetone on bromoform.

Actions and Uses .- Brometone is claimed to have the sedative action of the bromides without the disadvantage of producing bromism. In doses of 0.3 gramme (5 grains) four or five times a day, in adults, it is claimed to cause no unpleasant results and to produce no disturbance of the digestive organs, and to have no appreciable effect on the secretions. Its action is prompt and its effect is manifest for several hours. In doses exceeding 1.6 grammes (25 grains) daily it may produce dizziness, vertigo, anorexia, and mental hebetude, all of which symptoms disappear on discontinuance of its use. Therapeutically it has been recommended in mild conditions of excitation and insomnia, in so-called narcotic abstinence, in hysteria, and in nervous affections generally. It relieves some forms of cough and is said to produce amelioration in about 60 per cent, of cases of epilepsy. It has been used to relieve dizziness due to labyrinthine disturbances. Dosage.—The dose is 0.3 gramme (5 grains), to be repeated two or three times during twenty-four hours. Manufactured by Parke, Davis & Co., Detroit, Mich.

BROMIPIN.

A bromine addition product of sesame oil, containing 10 per cent. of bromine in organic combination.

Actions and Uses.—Bromipin acts like the bromides, but as it yields its bromine more slowly it is thought to have less tendency to produce brominism. The combination is not broken up in the stomach, but a portion of the bromine is split off as soon as the oil enters the intestine. The oil with the remaining bromine is easily absorbed, and, similarly to other fats, is largely deposited in the tissues, where it is slowly split up. It is said to be more lasting in its action than the bromides. Dosage.—4 c.c. (I fluidrachm), increased in cases of epilepsy to from 8 to 32 c.c. (2 to 8 fluidrachms); in emulsion with peppermint water and syrup, or pure, flavored with oil of peppermint. Manufactured by E. Merck, Darmstadt. (Merck & Co., New York.)

BROMIPIN-33 1/3 PER CENT.

A 33½ per cent. brominized sesame oil. Manufactured by E. Merck, Darmstadt. (Merck & Co., New York.)

BUTYL-CHLORAL HYDRATE.

Actions and Uses.—Its action is similar to that of chloral, except that it is said to be less depressing and more analgetic. It has been especially recommended for facial neuralgia. Dosage.—0.3 to 1.3 grammes (5 to 20 grains).

CALCIUM ICHTHYOL.

A derivative of ichthyol in which calcium is substituted for ammonium. Manufactured by the Ichthyol Company, Hamburg. (Merck & Co., New York.)

CALOMELOL.

A soluble colloidal form of calomel, containing albuminoids.

Actions and Uses.—Its action is the same as that of calomel, but it is claimed to be superior because of its solubility in water, acting more rapidly and efficiently. Calomelol is claimed to be non-irritant and particularly non-toxic. The indications for its use are the same as for calomel. Dosage.—Internally the same as calomel. Externally it is used as a dusting powder, mixed with an equal quantity of starch or of a mixture of starch and zinc oxide, or in the form of calomelol ointment. It should be guarded from the light. Manufactured by the Heyden Chemical Works, New York.

CALOMELOL OINTMENT.

Actions and Uses.—It is a substitute for mercurial ointment, over which it has the advantage of cleanliness, and it is claimed to be distinctly superior as an inunction in syphilis, etc. Dosage.—6 grammes (90 grains) daily for inunction in syphilis. Manufactured by the Heyden Chemical Works, New York.

CASCARA EVACUANT.

A preparation said to contain a bitterless glucoside, obtained from the bark of *Rhamnus Purshiana*, with aromatics.

Actions and Uses.—It is claimed that this preparation possesses the laxative properties of cascara sagrada without the bitterness which characterizes the ordinary extract. It is recommended for the treatment of chronic constipation, for which cascara sagrada is one of the best medicinal agents. Dosage.—As a laxative, 0.6 to 1 c.c. (10 to 15 minims) three times a day; as a purgative, 1.3 to 2 c.c. (20 to 30 minims) morning and evening. Four cubic centimeters (1 fluidrachm) may be given in obstinate cases. Prepared by Parke, Davis & Co., Detroit, Mich.

CASCARA TONIC LAXATIVE GLOBULES.

Each globule is said to contain 0.2 gramme (3 grains) of the bitter glucosides of *Rhamnus Purshiana* suspended in a bland fixed oil, to which aromatics have been added.

Actions and Uses.—The manufacturers claim that it combines the laxative action of cascara with tonic properties of the bitter principle with the advantage of concealment of the disagreeable taste. Dosage.—One or two globules to be taken before retiring. Prepared by Parke, Davis & Co., Detroit, Mich.

CHINAPHENIN.

Chinaphenin, $CO(NH\cdot C_6H_4OC_2H_5)(C_{20}H_{23}N_2O_2) = C_{20}H_{33}N_3O_4$, the quinine carbonic acid ester of phenetidin.

Actions and Uses.—Chinaphenin combines the antiperiodic properties of quinine with the analgesic power of phenacetin, with the advantage of tastelessness and asserted freedom from symptoms of cinchonism produced by the administration of the two remedies in simple mixture. It is recommended in febrile diseases, especially la grippe; in spasmodic conditions, such as whooping-cough; in certain forms of malaria and in neuralgia. Dosage.—Adult: 0.3 to 0.6 gramme (5 to 10 grains) ordinarily, 1.5 to 2 grammes (22 to 30 grains), given in two doses as an antipyretic in neuralgia and malaria; in whooping-cough: 0.13 to 0.3 gramme (2 to 5 grains), according to age. Manufactured by Farbenfabriken, vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color & Chemical Co., New York).

CHLORBUTANOL.

Chlorbutanol, I,I,I - trichlor - 2 - methyl - propan - 2 ol, $CCl_4\cdot C$ (OH) $(CH_3)\cdot CH_3 = C_4H_7OCl_3$, produced by the reaction of acetone on chloroform.

Actions and Uses.—It is said to be absorbed unchanged, but to

be decomposed in the body. It is a local anesthetic with an action weaker than that of cocaine, but sufficient to prevent vomiting from gastric irritation. Its antiseptic action is said to be fifteen times as strong as that of boric acid. It acts on the central nervous system similarly to chloral, and although the claim has been made that hypnotic doses are without effect on the circulation and respiration, independent observers have described a fall of blood pressure and interference with respiration in animals, and consider it fully as dangerous as chloral. In man 100 grains caused severe symptoms, but recovery occurred. It is claimed that no habit is induced, but this may be referable to its restricted employment. It is recommended as a mild local anesthetic, in dentistry, etc., as a preservative for hypodermic solutions, for insomnia, vomiting and for spasmodic conditions. It is also said to be useful as introductory to general anesthesia, lessening excitement and nausea. Dosage.-The dose is from 0.3 to 1.5 gramme (5 to 20 grains) dry or in capsules. Hypodermically as a local anesthetic a saturated aqueous solution may be used.

CHLORETONE.

A name applied to chlorbutanol, which see. Manufactured by Parke, Davis & Co., Detroit, Mich.

CHLORETONE INHALANT.

A solution of chloretone, camphor, menthol and oil of cinnamon in liquid petrolatum.

Actions and Uses.—An anodyne, antiseptic, and emolient solution for use by inhalation as a very fine spray or nebula. Manufactured by Parke, Davis & Co., Detroit, Mich.

anhydromethylene-citric acid.

Actions and Uses.—This is one of the compounds which it is claimed increase the elimination of uric acid by forming very soluble

compounds with that substance. It has been recommended for gout and chronic rheumatism. Dosage.—I to 2 grainmes (15 to 30 grains), largely diluted with water. Manufactured by Farbenfabriken, vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color & Chemical Co., New York).

CREOSOTAL.

A mixture of carbonic acid esters, analogous to guaiacol carbonate, prepared from creosote.

Actions and Uses.—Creosotal has the same action as creosote, but is claimed to be non-toxic and devoid of irritant properties. It is recommended as a substitute for creosote for internal exhibition in tuberculosis, pneumonia, and as an intestinal antiseptic. Dosage.

—From 0·3 to 2·0 grammes (5 to 30 grains) for children, to I to 4 grammes (15 to 60 grains) for adults in milk, coffee, wine, cod-liver oil or emulsion. Externally it may be applied undiluted. Manufactured by Farbenfabriken, vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color & Chemical Co., New York). Fabrik von Heyden, Radebeul, near Dresden.

DENTALONE.

A 30 per cent. solution of chloretone in a mixture of oils of gaultheria, cloves and cassia.

Actions and Uses.—Dentalone possesses pronounced anesthetic properties and is intended for use by dentists in the treatment of exposed nerves in decayed teeth. Prepared by Parke, Davis & Co., Detroit, Mich.

DERMATOL.

A name applied to Bismuthi Subgallas, U. S. P. Manufactured by Meister, Lucius & Bruening, Hoechst a. M. (Victor Koechl & Co., New York).

DIABETIN.

A pure, crystallized fructose (levulose), $CH_2OH \cdot CHOH \cdot CHOH$. $CHOH \cdot CO \cdot CH_2OH = C_6H_{12}O_6$, absolutely free from dextrose (ordinary glucose).

Actions and Uses.—Levulose is metabolized in the body by other agencies than those that act on dextrose and most of the other sugars and appears to be more completely utilized by the diabetic organism than the other sugars. It is recommended for the nutri-

tion and for sweetening the food and drink of diabetics, in pulmon. ary tuberculosis, infantile malnutrition and marasmus. Dosage:-It is given in diabetes in daily quantities of 30 to 60 grammes (1 to 2 ounces); in grave forms of the disease the amount is reduced to from 12 to 24 grammes (3 to 6 drachms) daily. Manufactured by Chemische Fabrik auf Actien, vorm. E. Schering, Berlin (Schering & Glatz, New York).

DIONIN.

Dionin, $C_{17}H_{17}NO(OH)$ (OC₂H₅HCl) + H₂O = ($C_{19}H_{21}O_3ClN$ + H₂O), the hydrochloride of the ethyl ester of morphine.

Actions and Uses.-It is claimed that this compound acts like morphine without producing constipation, nausea or lassitude. It is the conclusion of some good observers that it possesses no advantage over codeine. Applied to the eye, it causes a local vasodilation, leading to acute conjunctival edema. Dionin is recommended to relieve pain, especially in respiratory affections, as an antispasmodic in whooping-cough, for insomnia and externally in treatment of corneal affections, conjunctivitis, iritis, etc. Dosage.—0.015 to 0.06 gramme (1/4 to I grain). Externally it is applied in 10 to 20 per cent. solutions. Manufactured by E. Merck, Darmstadt. (Merck & Co., New York.)

DIURETIN.

A name applied to theobromine-sodium salicylate, which see, Manufactured by Knoll & Co., Ludwigshafen, Germany (E. Merck & Co., New York).

DUOTAL.

A name applied to Guaiacolis Carbonas, U. S. P. Manufactured by Farbenfabriken, vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color & Chemical Company, New York).

DUOTONOL.

A name applied to a mixture of equal parts of calcium tonol and sodium tonol. (See Tonols.)

Actions and Uses and Dosage. See Glycerophosphates. Manufactured by Chemische Fabrik auf Actien, vorm. E. Schering, Berlin (Schering & Glatz, New York).

ELIXIR EUPNEIN.

A preparation said to contain in each dose of 8 c.c. (2 fluidrachms): heroin 0.0026 gramme (1/24 grain), terpin hydrate 0.13 gramme (2 grains) creosote 0.3 gramme (5 grains), in a menstruum containing 30 per cent. of alcohol with glycerin and aromatic essential oils.

Actions and Uses.—From its composition it appears to be well adapted to use in chronic cough from bronchitis, etc. Dosage.—4 to 12 c.c. (I to 3 fluidrachms). Prepared by Schieffelin & Co, New York.

ELIXIR SAW PALMETTO.

An elixir of saw palmetto berries, sandal wood and cornsilk.

Actions and Uses.—The constituents of this preparation are credited with diuretic properties and believed to be sedative to the genito-urinary tract and to exert a curative action on the inflamed mucous membrane, especially in chronic cases. Dosage.—4 to 16 c.c. (I to 4 fluidrachms) three times a day. Prepared by Parke, Davis & Co., Detroit, Mich.

EMPYROFORM.

A condensation product of birch tar and formaldehyde.

Actions and Uses.—Empyroform is an antipuritic, sedative and desiccant. It is said to be superior to tar and free from irritant or toxic effects. It is claimed to be useful in all stages of eczema, psoriasis, lichen, urticaria, prurigo, pityriasis, etc. Dosage.—It is applied as a 5 to 10 per cent. ointment, 10 to 20 per cent. zinc paste, 10 to 20 per cent. tincture, and 37.5 per cent. suspension. Manufactured by Chemische Fabrik auf Actien, vorm. E. Schering Berlin (Schering & Glatz, New York).

EPICARIN.

Epicarin, C_6H_3 (OH) (COOH) (CH $_2C_{10}H_6OH$) 2: 3: $I=C_{18}H_{14}O_4$, β -naphthol-hydroxy-toluic acid.

Actions and Uses.—Epicarin is a non-poisonous antiseptic and parasiticide. Administered internally, it is excreted mostly undecomposed. It has been found useful in the treatment of skin-diseases, particularly scabies, tinea tonsurans, prurigo and certain forms of eczema. Dosage.—It is used externally only in the form of 5 to 20 per cent. ointment, with petrolatum or wool fat (lanolin) as base,

or in the form of oily or alcoholic solutions (10 per cent.). Manufactured by Farbenfabriken, vorm. Friedr. Bayer & Co., Elberfeld, Germany (Continental Color and Chemical Co., New York.

ERYTHROL TETRANITRATE.

Erythrol tetranitrate, $(C_4H_6(NO_3)_4 = C_4H_6O_{12}N_4$, the tetranitrate of erythrite or butane-tetrol, $(C_4H_6(OH)_4)$.

Actions and Uses.—It is a vasodilator and antispasmodic, like nitroglycerin. Its action is slower and more lasting; it begins in 15 minutes and persists for three or four hours. It is recommended in angina pectoris and cardiac diseases. It is reported as especially useful as a prophylactic in preventing anginal pain. Dosage.—Because of its explosiveness it is marketed in the form of tablets, each containing 0.03 gramme (½ grain). One or two tablets every four to six hours. Manufactured by E. Merck, Darmstadt (Merck & Co., New York).

ETHYLENEDIAMINE.

Ethylenediamine, C₂H₄ (NH₂)₂, a substitution compound of ethylene and ammonia.

Actions and Uses.—It is said to be non-corrosive. It is recommended as an albumin solvent for the solution of false membranes in diphtheria and similar affections of the mucous membranes. It is recommended for use in the form of kresamine (which see). Manufactured by Chemische Fabrik auf Actien, vorm. E. Schering, Berlin (Schering & Glatz, New York).

EUCAINE.

The "Eucaines" are two closely allied synthetic bases, which were originally differentiated as eucaine "A" and eucaine "B," but are now designated as "Alpha eucaine" and "Beta eucaine," respectively, alpha-eucaine being a synthetic derivative of triacetonamine, while beta-eucaine is a synthetic derivative of vinyl-diacetonekalmine. Both of these bases are supplied as hydrochlorides and are recommended as substitutes for cocaine, over which they are claimed to have certain advantages. They are described under alpha-eucaine hydrochloride and beta-eucaine hydrochloride.

(To be continued.)

Report of the Council on Pharmacy and Chemistry, from the Journal A. M. A., October 20, 1906.

TYREE'S ANTISEPTIC POWDER.

Tyree's antiseptic powder was assigned for examination to a subcommittee of the Council, which made the following report:

To the Council on Pharmacy and Chemistry: Your subcommittee, to whom was assigned Tyree's Pulv. Antiseptic Comp., marketed by J. S. Tyree, Washington, D. C., reports as follows:

The label on the package states: "This preparation is a scientific combination of borate of sodium, alumen, carbolic acid, glycerin and the crystallized principles of thyme, eucalyptus, gaultheria, and mentha, in the form of a powder," etc.

The statement that the powder contains the crystalline principles of thyme, eucalyptus, gaultheria and mentha is vague and misleading, since the chief medical constituents of eucalyptus and gaultheria are liquids, but it tends to convey the impression that the powder contains the essential constituents of these drugs, namely, thymol, oil of eucalyptus or eucalyptol, oil of wintergreen, or methyl salicylate, and menthol.

The literature supplied to physicians claims its composition to be: "Parts, sod. bor., 50; alumen, 50; ac. carbol., 5; glycerin, 5; the cryst. principles of thyme, 5; eucalyptus, 5; gaultheria, 5, and mentha, 5."

The composition, therefore, might be expressed as follows:-

Sodium borate	(bora	x)				٠						50	parts,	or	38.46	per	cent.
Alum												50	parts,	or	38.46	per	cent.
Phenol (carbol	ic acid	1)						٠				5	parts,	or	3.85	per	cent.
Glycerin .			.0									5	parts,	or	.3.85	per	cent.
Thymol												5	parts,	or	3.85	per	cent.
Oil of eucalypt	us or	eu	ca	1y	pt	ol						5	parts,	or	3.85	per	cent.
Oil of gaulther	ia (or	m	en	tl	ıy.	1 5	sal	lic	y1.	ate	e)	5	parts,	or	3.85	per	cent.
Menthol												5	parts,	or	3.85	per	cent.

Analysis of specimens purchased from different sources in the open market were made under our direction. The reports of the chemists show that Tyree's antiseptic powder contains no borax, or mere traces only, and that it contains no alum, or mere traces only. Instead, the analyses show that boric acid and zinc sulphate are the essential constituents. The amounts of carbolic acid, thymol, men-

thol, etc., contained in the powder, if present, were far below the quantities indicated by the formula. The presence of glycerin could not be demonstrated, and if present the amount must be very small.

Our chemist reports:-

The result of analysis shows that different samples differ slightly in composition, but that the following indicates the average composition of the product:—

																		Per cent.
Zinc sulphate,	an	hy	/d	rot	18													15.56.
Boric acid										*								81.26.
Volatile matter	at	T	00	C.	f	or	fo	ur	h	101	irs							0.45.

The undetermined portion consists of salicylic acid, carbolic acid, menthol and eucalyptol; possibly other antiseptic agents may be present in very minute quantities.

From the above findings we conclude that Tyree's antiseptic powder is a mixture of boric acid and dried zinc sulphate and antiseptic bodies, such as menthol, salicylic acid and carbolic acid, eucalyptol, etc. From this it can be readily seen that the label which is supposed to set forth the composition of Tyree's antiseptic powder is not in accord with the facts. The powder does not contain either borate of sodium or alum, and the presence of glycerin could not be established. The antiseptic agents, exclusive of the boric acid, are present only in small amounts.

The report of another analyst concludes as follows:

It evidently contains less than the amount stated of the principles of thyme, eucalyptus, wintergreen and mint. It also contains a very small amount indeed of carbolic acid, much less than that stated. We have been unable to identify certainly the presence of glycerin, and it is doubtful if it be present.

From the result of the analysis we feel confident that the preparation is to all intents and purposes a mixture of boric acid and sulphate of zinc.

The carbolic acid, thyme, eucalyptus, wintergreen, etc., if present, are present only in sufficient amount to give the compound a satisfactory odor.

In view of the fact that J. S. Tyree has given wide publicity to a formula which the preceding report has shown to be a deliberate misrepresentation of fact, it is recommended that the article be refused recognition by the Council on Pharmacy and Chemistry, and

that this report be published in the Journal of the American Medical Association.

The recommendation of the subcommittee was adopted by the Council in accordance with which the report is published.

W. A. PUCKNER, Secretary.

In a letter to the editor of the Journal of the American Medical Association, Mr. Tyree admits changing the formula of the powder, and says that it had been his intention to state to the medical profession his reasons for making the change. In commenting on the letter it is noted that Mr. Tyree does not state whether the change was made one year ago or five years ago, but the sample for the first analysis was purchased last February, and the first chemist's report was submitted to the Council March 5, 1906. On April 4th, Mr. Tyree was notified by the Council that the composition of "Tyree's Antiseptic Powder" did not correspond with the formula published by him. Whether or not Mr. Tyree is justified in offering to physicians a preparation as composed chiefly of borax and alum, when in reality it is composed of boric acid and zinc sulphate, is left for physicians to judge.

FRAUD AND DECEPTION IN PREPARATIONS OF COD-LIVER OIL.

The Journal of the American Medical Association, October 13, 1906, exposes the fraud and deception practised by certain proprietary firms in putting on the market preparations purporting to contain cod-liver oil, when, in fact, they contain no oil at all. It is conceded by pharmacologists that the value of these remedies depends on the nutritive power of the fat, and any preparation which contains fat must respond to simple tests which the physician can personally apply. The preparations claiming to represent cod-liver oil are in liquid form, and if they contain oil it must be in one of the following forms:

- (1) An emulsion of the oil which may be miscible with water, but from which the fat tends to separate and rise to the top. In this form the fat can be seen as globules under the microscope.
- (2) A solution, resulting from the saponification of the oil, containing a soap which usually will be alkaline in reaction, especially when mixed with water, and from which fatty acids are separated as a precipitate when the solution is acidified.

(3) A solution of fatty acids. This will be acid in reaction and will be precipitated by the addition of water, in which the fatty acids are not soluble.

An examination of one of these preparations, e. g., Waterbury's Metabolized Cod-Liver Oil, which, it is claimed, "contains the metabolized product obtained by the action of ferments on cod-liver oil," shows that it is neither an emulsion, a solution of soap, nor a solution of fatty acids, and more careful analysis shows that it contains no fat or fat acids (except the merest traces). No intelligent physician should be misled by the extravagant and unfounded claims made for this preparation.

Hagee's Cordial of Cod-Liver Oil is a representative of a class of preparations which claim to "represent the oil, but contain no fat," and are therefore practically worthless. The claims of therapeutic value for such preparations can not be substantiated. Some such remedies are advertised as extracts of cod-liver oil, when, in fact, they are made from cod livers, but not from cod-liver oil. These preparations, if honestly made, might be worthy of a trial, but they are not preparations of cod-liver oil, and should not be so termed. So far as we know, however, no satisfactory evidence is forthcoming that such extractives have any therapeutic value.

The attempt to modify cod-liver oil for therapeutic purposes may be pronounced a failure and the large variety and extensive sale of these preparations appear to be owing to the fact that physicians do not recall the ordinary facts of chemistry, but accept too readily the statements of the manufacturers.

PROGRESS IN PHARMACY.

A QUARTERLY REVIEW OF SOME OF THE MORE IMPORTANT ADVANCES
IN PHARMACY AND MATERIA MEDICA.

By M. I. WILBERT,

Apothecary at the German Hospital, Philadelphia, Pa.

The Food and Drugs Act, June 30, 1906, continues to be the leading topic for discussion in pharmaceutical journals and in pharmaceutical circles generally. In many of the larger cities special meetings have been held at which the probable effect of the law,

directly as well as indirectly, on the several branches of pharmacy have been discussed at length.

Wholesale druggists and manufacturing pharmacists appear to be heartily in favor of the underlying principles and of the general provisions of the Federal pure food and drug law, despite the fact that it has imposed an enormous amount of additional work and expense for which they can scarcely expect to be adequately recompensed.

The proposition to endorse the Federal law, by corresponding laws in the several States, has aroused considerable opposition on the part of retail pharmacists, who appear to be either indifferent or else fearful lest the additional obligations that would be imposed on them might be too exacting or else involve an undue amount of work or expense to comply with.

In this connection we should remember that pharmacists, as such, have taken little or no part in securing the enactment of the Federal pure food and drug law, and that, as a consequence, they have thus sacrificed no little of their professional independence and prestige.

This apathy on the part of pharmacists is even now being taken advantage of by members of boards of health, Food and Dairy Commissioners and well-meaning but frequently misinformed reformers who are actively at work to secure food and drug legislation along the lines of the National law.

In by far the greater number of State legislatures, now in session, bills for laws of this kind have been introduced, and whether enacted into laws or not, will tend to show the wants or desires of retail pharmacists, and, if opposed or ignored, will seriously reflect on the ability and professional disinterestedness of pharmacists themselves.

Retail pharmacists should, and if they desire to maintain their standing in the community they must, favor pure food and drug legislation that is designed to protect the public. By themselves taking an active interest in the securing of legislation along these lines they could readily prevent the enactment of ill-advised measures that would tend to hamper or restrict them in the pursuance of their business.

That the medical profession in all sections of the country is clearly in favor of pure food and drug legislation was plainly evidenced at the Conference of the Committee on Medical Legislation, of the American Medical Association, with the National Legislative Council, held at Washington, D. C., December 13th to 15th inclusive.

State legislation was discussed at some length and the representatives of the several State Medical Associations who were present expressed themselves in no uncertain way as being in favor of the individual States endorsing the Federal Food and Drugs Act.

The proceedings of this conference have been published in pamphlet form, comprising sixty-eight pages of closely printed material. This pamphlet contains much that is of interest to pharmacists, and may be obtained from the Secretary of the Bureau of Medical Legislation of the American Medical Association, 103 Dearborn Avenue, Chicago, Ill.

The available literature on pure food and drug legislation is rapidly assuming huge proportions. In addition to the liberal space that is devoted to the question in the current numbers of pharmaceutical journals, a number of reprints of material of this kind have appeared. Not the least interesting of these reprints is a pamphlet of sixty-four pages entitled:—

The Food and Drug Act as it relates to drugs, examined and explained in connection with the rules and regulations for its enforcement. This pamphlet is published by the National Druggist, St. Louis, Mo., and contains in addition to the law itself and the regulations pertaining to it, a number of interesting decisions and much additional material bearing more or less directly on the proper interpretation of the Food and Drugs Act.

Digest of National Food and Drugs Act and Regulations, by Mahlon N. Kline, is the title of a pamphlet containing upwards of seventy-two pages that has recently been sent out with the compliments of the Smith, Kline, French Company, Philadelphia. In addition to a transcript of the Food and Drugs Act, and of the rules and regulations for the enforcement of the same, this pamphlet also contains a number of additional opinions, replies and explanations that have been published from time to time; also a legal exposition of the Food and Drugs Act by George L. Douglas, attorney for the Proprietary Association of America; extracts from the recently published "Standard of Purity for Food Products," and much additional information of interest to retail pharmacists.

The Ladies' Home Fournal Bill, or a corresponding measure to regulate the manufacture and sale of so-called patent medicines, has

been introduced in upwards of ten of the State legislatures now in session. This bill, originally published in the *Ladies' Home Journal* about a year ago, is essentially a formula on the label bill and provides, in addition, that preparations containing one or more of certain specified drugs be labeled *poison*.

Anti-narcotic legislation is also receiving a fair proportion of attention. The most drastic of these measures is probably the one that has been introduced into the legislature of the State of New York, at the instance of the Evening Journal. This bill prohibits the sale of opium, chloral, cocaine, eucaine or acetanilid, or any preparation containing them, except on the original written prescription of a physician, dentist or veterinarian.

In several States, notably Texas and Missouri, bills are pending that are designed to improve or to revise the laws governing the practice of pharmacy.

Patent Reform Bill.—Representative Currier, Chairman of the House Committee on Patents, has introduced a bill to substitute the much discussed Mann bill. This bill, popularly known as the Currier bill, is practically a revival of the reciprocity feature of the original Mann bill, but is not restricted to medicine, or medicinal products and includes patents of all kinds.

The Currier bill provides: "That any patent issued to a citizen or subject of a foreign country, shall be upon the same conditions and for the same term as are patents issued by such country to citizens of the United States."

This single provision, it is said, would effectually correct the evils arising from our present system of process and product patents, but would be contrary to the terms of the International Convention for the protection of industrial property and will no doubt be vigorously opposed on this ground.

Incorporation of the Public Health Defense League. A bill has been introduced into the Legislature of the State of New York providing for the incorporation of the Public Health Defense League, under a special charter patterned after that of the Red Cross Society.

The object of this new society is announced as being an organized movement against medical and surgical quacks, frauds in patent medicines or nostrums, and an effort to obtain and to disseminate accurate information concerning practices and conditions of every kind that are dangerous to the public health and morals. (Fournal A. M. A., 1907, page 236.)

Sunday Rest in France.—Pharmacists in France are not alone adapting themselves to the recently enacted Sunday Rest Law, but are even going farther and are adopting earlier hours for closing during the week.

At Grenoble, where Sunday closing has been in vogue for some time, the pharmacists have decided to close at 8 p.m. daily and to organize a night service by rotation.

The syndicate of Paris pharmacists recommends that its members adopt 9 P.M. as the hour for closing during the week and to close from midday till the following morning on Sundays and bank holidays. (Chem. and Drug., 1906, page 775.)

Popularity of Pasteur in France.—The Petit Parisien has taken a rather interesting plebiscite as to who is thought to be the greatest of nineteenth century Frenchmen. In the voting Pasteur took the lead from the first, followed by Victor Hugo, Gambetta, Napoleon I, Thiers and Lazare Carnot, in the order named. (Chem. and Drug., 1907, page 6)

Doses in the Codex — The Codex Revision Committee has decided to include a list of maximum doses in a supplement to the Codex, and has delegated the work of drawing up such a list to a special committee including MM. Laudouszy, Marty, Bourquelot, Gilbert and Yvon. (Chem. and Drug., Dec., 1906, page 884.)

The Druggists' Circular has rounded out a half century of its existence. The January, 1907, number of this journal constitutes a fiftieth anniversary number and comprises a total of 320 pages. The 190 or more pages that are devoted to reading matter contain quite an exhaustive review of American pharmacy during the past fifty years. All of the more interesting articles are liberally illustrated and the number itself will no doubt be appreciated as an album of men who have contributed, or are now contributing, to the development of the science of pharmacy in America.

Incompatibility of Pepsin and Pancreatin in liquid preparations.—
A report of the Council on Pharmacy and Chemistry of the American Medical Association (Fournal American Medical Association, February 2, 1907, p. 434) calls renewed attention to the generally well known fact that despite the frequently made statement that pepsin and pancreatin must be incompatible in liquid preparations

a number of such mixtures are still being offered by manufacturers or retail pharmacists and are used by physicians.

The Council has investigated a number of preparations of this type and has invariably found them to be practically inert in at least some of the claims made for them. Having demonstrated that pepsin and pancreatin cannot exist in one and the same solution for any reasonable length of time and that preparations that are said to contain these two ferments are sold under impossible claims, the Council recommends:

- (1) That the Council on Pharmacy and Chemistry refuse to approve liquid preparations that are claimed to contain both pepsin and pancreatin.
- (2) That the medical profession through the Journal of the American Medical Association be advised of the fallacy of employing such combinations.
- (3) That the attention of manufacturers be called to the worthlessness of such incompatible liquid preparations of pepsin and pancreatin and that they be urged to cease offering such products to the profession.
- (4) That since the National Formulary has recognized a preparation of this kind under the title "Elixir Digestivum Compositum" the American Pharmaceutical Association be requested to instruct its committee on the National Formulary to omit this preparation from the next edition.

Acetanilid Muxtures.—The mixtures of acetanilid and other ingredients that formerly were exploited as definite chemical compounds are now being marketed as mixtures, and, in some cases at least, have had their composition changed so as to be totally unrecognizable.

Antikamma, under the regulations of the Pure Food and Drugs Act, is being marketed as a mixture containing 350 grains of acet-phenetidin in each ounce. Pharmacists who are in the habit of filling prescriptions for physicians calling for "antikamnia" in solution will now experience the additional difficulty of being obliged to explain why the new antikamnia differs from the old in its physical properties.

Ammonol.—This preparation is said to be Ammoniumphenylacetamid on one portion of its label and directly under it is said to contain 240 grains of paracetyl-phenetidin in each ounce.

Phenalgin, marketed as an ammoniated phenylacetamide, is labeled as containing 50 per cent. of acetanilidum.

Benzosalin.—Methyl benzoyl salicylate occurs as a white crystalline powder having a slight aromatic odor and taste. The substance melts at from 84 to 85° C. It is nearly insoluble in water, but is soluble in 35 parts of alcohol and is readily soluble in chloroform but somewhat less so in ether. (Phar. Centralh, 1906, p. 1053.)

Borovertin.—This is the name that has been applied to hexamethylene tetramine triborate. The substance occurs as a yellowish white powder readily soluble in water and having a distinctly bitter taste. It may be given in doses of from I to 4 grammes daily. (Phar. Centralh., 1906, p. 928.)

Castor oil in form of powder.—A recently issued German patent describes a process for preparing a supposedly active preparation of castor oil in powder form. This is accomplished by the addition of light calcined magnesia to an emulsion of castor oil, or by adding a specific quantity of castor oil to the same weight of calcined magnesia that has been moistened with distilled water, and drying the resulting mixture and powdering the residue. (Phar. Centralli, 1907, p. 65.)

Cystopurin.—This is said to be a combination of one molecule of hexamethylene tetramine with two molecules of sodium acetate. It occurs as white, nearly tasteless crystals that are readily soluble in either hot or cold water. Cystopurin may be administered in doses of 1 or 2 grammes three times a day. (Phar. Zeit., 1907, page 48.)

Forgenin.—This is said to be tetra methyl ammonium formiate and responds to all of the known reactions for formic acid compounds. It is being recommended, in small doses, as a heart tonic. (Phar. Zeit., 1907, page 48.)

Levurinose is a name given to a yeast that has been desiccated by means of a current of cold air so as to preserve the individual yeast cells intact. This preparation has been recommended to be used in affections of the skin, such as acne, eczema, furunculosis, urticaria, etc. (Phar. Zeit., 1907, page 47.)

Mistura Strzyzowski is the formidable name, applied in Austria, to a mixture containing ferric pyrophosphate, quinine hydrochloride and sodium bromide. This mixture is directed to be prepared as follows:—

Sodium bromide 8.00 is dissolved in distilled water, 40.00; syrup

of orange peel, 2000; alcohol, 1000. Mix and add a solution of quinine hydrochloride, 1000 in distilled water, 4000; and syrup of orange peel, 2000. Mix, and then add the following, prepared by slightly warming: Ferric pyrophosphate with ammonium citrate, 400 in distilled water, 4000. Mix, and add syrup of orange peel, 4000.

Dose, one to two teaspoonfuls, with water, two or three times a day.

Novaspirin is the name applied to methyl citric acid ester of salicylic acid. It occurs as a white powder having a slightly acid taste. It is nearly insoluble in water but is readily soluble in alcohol. Novaspirin may be given in doses of I gramme three times a day. (Phar. Zeit., 1907, page 9.)

Quinine Phytinate.—Anhydro oxymethylene diphosphate of quinine occurs as a yellow powder, very soluble in water but almost insoluble in alcohol, ether, benzin or chloroform. The substance contains 57 per cent. of quinine and has an intensely bitter taste.

Scarlatin Marpman is an antitoxin preparation that, given internally, is being used as a prophylactic for scarlet fever. It is said to be produced by inoculating animals with infectious material from scarlet-fever patients and inoculating other animals with the serum taken from the first. The serum from the blood of the second animal is used to immunize other animals, and it is from these immunized animals that the antitoxin serum is prepared.

Scarlatin is a yellowish, opalescent liquid having a slight odor and a salty taste. The substance has a specific gravity of from I-012 to I-013, is neutral in reaction and gives a copious precipitate with reagents for albumin. (*Phar. Centrall.*, 1907, page 69.)

Solubility of Salicin.—D. B. Dott (Phar. Four., 1907, page 79) finds that the solubility of salicin, as given in the British Pharmacopæia (I in 28) is practically correct, while that of the U. S. P. (I in 21 at 25° C.) is too high.

Using pure salicin, that melted at 201° C., he finds that it has a solubility of 1 in 24 at 25° C., or very nearly that called for by the British Pharmacopæia at ordinary temperatures.

Substitutes for Cocaine.—Dr. Hugo Wintersteiner (Wiener Mea. Wochensch., 1906, page 1339) reports a comprehensive comparative study of the use of cocaine and its various substitutes in eye work. Of the numerous substances that have been proposed from time

to time he describes tropococain, holocain, eucain, stovain, alypin and novocain at some length and concludes that while it is true that these substances are relatively more stable than cocain, and are therefore more readily sterilized, the numerous objectionable features, such as unreliability, irritating properties and the production of a hyperemia, are so much more objectionable that cocaine must be admitted to be by far the most satisfactory as well as the safest local anesthetic in all varieties of eye work.

Tannisol is a reddish-brown, odorless and tasteless powder that is insoluble in water, ether or benzine, but is soluble in alcohol and in dilute solutions of alkalies or of the alkaline carbonates. It is directed to be used internally in cases of intestinal catarrh, and externally for a variety of inflammatory conditions of the skin, Internally it may be given in doses of 0.50 gramme (Phar. Centralh., 1906, page 1006).

Theolactin.—This name has been applied to a double salt of theobromin sodium and sodium lactate. It occurs as a white hygroscopic powder, readily soluble in water and having a distinctly bitter taste. It is said to be an active diuretic, but is not free from occasional side effects in the form of gastric disturbances. Zeit., 1907, page 49.)

Tinctura olea Europeae.—A tincture made with 60 per cent. alcohol from the dried leaves of the European olive has been used as a febrifuge as well as a general tonic in place of the tincture of cinchona bark.

Triacetyl morphin.—This substance has been isolated from a mixture of acetyl derivatives of morphin. Triacetyl morphin melts at from 206 to 208° C., is only slightly soluble in water or cold alcohol, but is readily soluble in acids. With hydrochloric acid it forms a salt that crystallizes in the form of long needles. (Phar. Centralk., 1906, page 928.)

Tulaselactin is the name given by Behring to a substance that is expected to immunize infants against tuberculosis. (Phar. Centralh., 1907, page 24.)

Tulase (A. J. P., 1906, page 582) is the name given by Behring to his immunizing and curative serum for tuberculosis.

This preparation is said to contain all of the constituents of the Koch bacillus. It occurs as a clear fluid which has the general outward characteristics of thin honey. It may be given subcutaneously, intravenously or by mouth. The mixture of tulase with milk, mentioned above, is the form in which it may be administered to infants.

Tulase is now being used in an experimental way, but Behring himself warns against too much reliance being placed on the curative properties of the substance.

CORRESPONDENCE.

Editor of the AMERICAN JOURNAL OF PHARMACY.

DEAR SIR:—I send you herewith the result of the votes of the Committee of Revision upon the first instalment of corrections in the U.S. Pharmacopæia, eighth revision, since the passage of the Food and Drugs Act.

Very truly yours,

JOSEPH P. REMINGTON, Chairman.

CHANGES AND CORRECTIONS IN THE UNITED STATES PHARMACOPOEIA.

(Eighth revision.)

Belladonna Leaf now 0.3 per cent. mydriatic alkaloids.

Belladonna Root now 0.45 per cent. mydriatic alkaloids.

Colchicum Seed now 0.45 per cent. of colchicine.

Ipecac now 1.75 per cent. of ipecac alkaloids.

Stramonium now 0.25 per cent. of mydriatic alkaloids.

Fluidextract of Belladonna Root now 0.4 gramme alkaloids in 100 c.c.

Tincture of Belladonna Leaf now 0.03 gramme alkaloids in 100 c.c. Fluidextract of Colchicum Seed now 0.4 gramme alkaloid in 100 c.c.

Tincture of Colchicum Seed now 0.04 gramme alkaloid in 100 c.c.

Fluidextract of Ipecac now 1.5 gramme alkaloids in 100 c.c. Fluidextract of Stramonium now 0.25 gramme alkaloids in 100 c.c.

Extract of Stramonium now 1.0 per cent. alkaloids.

Tincture of Stramonium now 0.025 gramme alkaloids in 100 c.c. Jalap Root now 7 per cent. of total resin.

Under the article Petrolatum, p. 336, U. S. P., last paragraph, the sulphuric acid test has been dropped.

February 15, 1907.

BOOK REVIEWS.

ELEMENTS OF GENERAL CHEMISTRY WITH EXPERIMENTS. By John H. Long, M.S., Sc.D., Professor of Chemistry and Director of the Chemical Laboratories in the Northwestern University Medical School. Fourth edition, revised and enlarged. Illustrated. Philadelphia: P. Blakiston's Son & Co., 1906.

That Professor Long was more than justified in writing this text-book is shown by the fact that since the appearance of the first edition in 1888 two other editions have been issued, and it has been necessary now to issue a fourth edition. The time has gone by in all of the sciences when it can be said that a student is acquainted with fundamental principles unless he has repeated some of the classroom work in the laboratory. As Dr. Long well says: "Repetition is necessary to fix elementary principles thoroughly in the mind of the beginner."

The present edition contains some additional matter on the theories of solution, the conditions of chemical equilibrium, some newer views of chemical theory and the description of several new substances. The book is a remarkably good one for the beginner, and is well adapted to the needs of the Freshmen class in any of the colleges where a general course in inorganic chemistry is given.

CHEMICAL ABSTRACTS. Published by the American Chemical Society.
Vol. I, Nos. 1 and 2. Easton, Pa.: The Chemical Publishing
Co. January 1 and 20, 1907.

Under this title the American Chemical Society has begun the publication of an independent semi-monthly periodical which shall furnish to American chemists at short intervals a full and comprehensive series of abstracts covering the whole range of pure and applied chemical science together with the titles of American, British, French and German patents on chemical subjects.

The importance and value of this undertaking can hardly be over-estimated. The Journal of the English Chemical Society has long covered somewhat similar ground, but hardly in the complete manner that our American society has now attempted; the Journal of the Society of Chemical Industry has always made a feature of its abstracts and patent references, but these cover applied chemistry only; the German Chemical Society some years ago took over the publication along with its Berichte of the Chemische Centralblatt

for this same purpose of furnishing a complete series of abstracts, but it was felt that our American Chemical Society should take up this work for its own membership, now numbering over 3000 chemists.

So the Society for the future will publish its Journal as a monthly for original papers and communications, of which it has as many as it can possibly find room for in its twelve issues, and the Abstract Journal as a semi-monthly, covering the whole field of pure and applied chemistry under some 30 subdivisions, of which pharmaceutical chemistry is one. That this subject will be cared for in an appreciative and intelligent way can be assumed, as we note that Prof. A. B. Stevens of Ann Arbor is in charge of the abstracts in this field. For those who are not members of the Society the subscription price is as follows: Journal of the American Chemical Society, monthly, \$6; Chemical Abstracts, semi-monthly, \$6; for both journals sent to the same subscriber, \$10. Members of the American Chemical Society receive both journals for the annual membership fee of \$8.

THE PHILADELPHIA BRANCH OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The regular stated meeting of the Philadelphia Branch of the American Pharmaceutical Association was held on the evening of Friday, January 4, 1907, and was attended by 63 members and visitors.

The minutes of the previous meeting were read and declared approved.

The Committee on Sunday Closing and the Committee on State Legislation made preliminary reports that were received and ordered filed.

On behalf of the Committee on State Legislation Mr. Cliffe said that members of the committee had had an opportunity to confer with the members of a special committee of the State Legislature on the subject and that a joint conference of members of committees interested in the enactment of a State Food and Drug Law would be held at the Philadelphia College of Pharmacy on the evening of Tuesday, January 15, 1907.

The regular program for the evening was then proceeded with. This consisted of a discussion of "The Debasing Influences of Fraudulent Nostrums."

The first communication, by Dr. Solomon Solis Cohen, was devoted to the consideration of "Secrecy and Fraud as Deterring Factors to the Progress of Medicine." Dr. Cohen, in the course of his remarks, said that progress means an ascent from little or no knowledge to knowledge, and from knowledge to greater knowledge. Secrecy is the withholding of knowledge and breeds ignorance, while fraud is even worse than ignorance in that it is designed to mislead.

Dr. Cohen also asserted that therapeutics was difficult enough under the most favorable conditions and that in cases where a physician is confronted with secrecy or fraud, in the statements made in connection with medicinal preparations, he is likely to be misled himself and to do untold harm to his patients.

In concluding, the speaker referred to a number of specific preparations which have been discovered to differ materially in composition from what was claimed for them. He also expressed the hope that the Federal Pure Food and Drugs Law would be instrumental in leading manufacturers to more duly appreciate the need for a greater degree of honesty in the exploitation of their wares. If pharmacy is to make progress and if medicine is to make progress it will necessitate a full and complete knowledge of the composition and action of the substances used in the treatment of diseases.

The next communication, by Dr. Henry Leffmann, dealt with: "Known and Unknown Changes in the Composition of well known Nostrums."

Dr. Leffmann said that the question of secrecy was one of the most intricate problems and one that involved a number of factors.

Secrecy in connection with nostrums, the composition of which was known only to some one or more individuals, but not to all was an objectionable feature and frequently led to arbitrary and in many instances dangerous changes in the composition and the action of nostrums.

Dr. Leffmann then called attention to a number of specific instances in which it was known that changes had been made in the composition of widely advertised nostrums and also pointed out how these changes might be injurious to the consumer. "Criminal Responsibility in the Sale of Abortifacients" was the subject matter of the communication by Dr. Henry Beates, Jr.

Dr. Beates referred to the various statutes relating to the use, sale or distribution of abortifacients and condemned, in no uncertain terms, the practice of advertising, in lay journals, articles designed to prevent conception or to produce abortion. He held that additional publicity might well be given to the serious nature of the questions involved, and urged that steps be taken to prevent the use of the United States mails by newspapers and magazines publishing advertisements of abortifacients or of instruments designed to prevent conception.

Dr. John B. Roberts, in opening the general discussion of the question, asserted that there certainly could be no difference of opinion on the degrading influences of practices that, as had been shown by the previous speakers, tended to convert pharmacists and pharmaceutical manufacturers into liars and medical practitioners into frauds and fakirs.

The subject matter was further discussed by Dr. Henry W. Cattell, Dr. F. E. Stewart, Dr. C. B. Lowe and Messrs. Remington, La-Wall, Turner, Thum, Beringer, Vanderkleed, Cable, Westcott, Wilbert and Cliffe.

Mr. Cliffe presented the following resolutions, which, on motion, were unanimously adopted:

Resolved that the Philadelphia Branch of the American Pharmaceutical Association condemns the advertisement in drug journals, magazines and newspapers of abortefacient medicines and deprecates their sale by reputable pharmacists.

Resolved that all members of this branch be urged to exclude such medicines and articles from their stocks.

The secretary then read a communication entitled "Objectionable Side Lines to the Practice of Medicine," specifically mentioning several profit-sharing and stock-distributing schemes that are now doing business in the city of Philadelphia.

This communication was, on motion, directed to be forwarded to the Secretary of the Philadelphia County Medical Society with the offer to submit additional evidence to the officials of that organization.

There being no further business the meeting was declared adjourned.

FEBRUARY MEETING.

The regular stated meeting of the Philadelphia Branch of the American Pharmaceutical Association was held on the evening of Tuesday, February 5, 1907, in the Hall of the College of Physicians.

The subject under discussion, "Higher Educational Requirements for Pharmacists," has attracted considerable attention during the past year or more, and it was therefore not surprising to find that retail pharmacists attending this meeting were comparatively well informed on questions relating to education, and fully appreciated the need for more rapid advancement along educational lines in the future.

The first speaker on the subject, Mr. William L. Cliffe, in discussing "The Practical Needs for Higher Education in Pharmacy," called attention to the fact that the people at large are rapidly becoming more thoroughly familiarized with the needs and the wants of the practice of pharmacy.

He believes that with the further elimination of empiricism and mysticism from the science of medicine more will be expected of pharmacists, and they in turn will be required to be educated in every way.

Prof. Henry Kraemer, in speaking on "Standards in Pharmaceutical Education," (see p. 101) called attention to the fact that up to the present time the progress of pharmacy in this country had been comparatively slow and that we are now entering on an era of more rapid development. He believes that the enactment of pure food and drug laws will add great additional responsibility to the duties of the retail pharmacist and will also tend to more sharply define the corresponding duties of the colleges and of the boards of pharmacy.

Dr. Horatio C. Wood, Jr., in speaking on "The Future Elaboration of a Course in Pharmacy," said that, as a commercial pursuit, the business of pharmacy must necessarily be one of limited scope and possibilities; as a profession, however, pharmacy can be developed into an occupation of laudable aims and high ideals. He believes that the pharmacist should develop as the assistant and the adviser of the physician, who in turn must depend more and more on the efforts of the pharmacist to select for him and to improve on the efficiency of the available articles of the materia medica.

Prof. I. V. S. Stanislaus, in opening the general discussion, gave it as his opinion that the pharmacist of the future would again hold the same relative position to the public as did the apothecary of old.

The pharmacist of the future will be the chemist of the people, the food and drug analyst, the assistant and adviser of the physician, in all matters relating to materia medica and chemistry, and will, therefore, practically be the sanitarian of the community.

The subject was further discussed by Messrs. John K. Thum, Franklin Apple, Jacob Eppstein, M. I. Wilbert, H. C. Blair, E. Fullerton Cook, John Hahn and Dr. F. E. Stewart. From the general trend of this discussion it was plainly evident that the better informed retail pharmacists deeply appreciate their responsibility to the public, and are willing and even anxious to meet their obligations fully. At no time in the history of pharmacy in this country has it been so evident that the mentally and morally poor man should not be allowed to jeopardize the health and even the lives of his fellow beings as now.

It is clearly evident that pharmacists are beginning to realize that a full and complete appreciation of their duties to society at large must of necessity react to their own pecuniary advantage and will in addition procure for them the respect and the admiration of their fellow men.

M. I. WILBERT,

Secretary.

A REVIEW OF THE OPSONINS AND BACTERIAL VACCINES.¹

By E. M. HOUGHTON.

As requested by the *Therapeutic Gazette*, I shall attempt to describe as succinctly as possible the theory of the opsonins and the therapeutic results that have been obtained by the application of the new theory. As the years go by we realize more thoroughly the correctness of the prophetic belief of the "Immortal Pasteur," that the day would come when it would be possible to eradicate the infectious diseases by vaccination.

We are indebted to Metchnikoff for calling attention to and explaining the rôle of the white blood cells in the defence of the body against bacterial invasion, but the phenomenon of phagocytosis is

¹ Reprinted from Therapeutic Gazette, January 15, 1907.

not so simple as it at first appeared, as little by little new facts are developed which amplify our knowledge of the subject.

It was shown by Denys and Leclef, in 1895, that when rabbits were immunized against *Streptococcus pyogenes* the serum acquired but slight bactericidal properties, but that such serum, when brought in contact with the leucocytes of normal or immunized rabbits, greatly enhanced their phagocytic activity. Conversely no acceleration of phagocytosis was observed when the corpuscles were brought in contact with the serum of a normal animal.

Mennes two years later confirmed this by showing that similar results were obtained from the blood serum of guinea-pigs treated with cultures or toxins of Pneumococci.

A method of measuring the phagocytic activity of the leucocytes was developed by Leishman in 1902. In 1903 Wright and Douglas made an extensive study of the phagocytes, when brought in contact with suspensions of *Staphylococcus pyogenes*, and were able to show:

- (1) Quoting from the original: "We have here conclusive proof that the blood fluids modify the bacteria in a manner which renders them a ready prey to the phagocytes. We may speak of this as an 'opsonic' effect (opsono [a Latin verb], I cater for; I prepare victuals for), and we may employ the term 'opsonins' to designate the elements in the blood fluids which produce this effect."
- (2) Normal blood serum and plasma possess the same opsonic action upon bacteria.
- (3) Serum loses its opsonic action when heated to 60° C. This is spoken of as inactivated serum.
- (4) Inactivated serum and physiological salt solution have the same influence upon phagocytosis.
- (5) "The opsonic power of the blood fluids disappears gradually on standing," losing about 50 per cent. of its activity in five or six days.
- (6) An anti-opsonic effect is noted when blood serum is digested with typhoid bacilli.
- (7) When a condition of immunity is conferred upon patients infected by Staphylococci, by vaccination with heated cultures of Staphylococci, the opsonic action of the patient's blood serum is greatly augmented.

Neufeld and Rimpau (1904) found in antistreptococcic and pneu-

mococcic sera evidence of substances which, while inactive towards leucocytes, possessed very marked opsonic or sensitizing action, as they termed it, toward corresponding cultures of streptococci and pneumococci.

Ross (Lancet, November, 1906) summarizes our knowledge of the opsonins as follows:

- "(1) Opsonins act by chemically uniting with the invading bacteria, and so altering them that the leucocytes are able to phagocyte the bacteria and destroy them. It is important to remember that these substances do not stimulate or otherwise affect the leucocytes.
- "(2) It is probable that there are present many varieties of opsonins in the blood plasma, each having to do with combating a particular kind of microbic invasion.
- "(3) Opsonins have been shown to be distinct from other bacteriotropic substances, such as the bacteriolysins, the agglutinins, and the antitoxins."

The leucocytes of healthy or diseased persons seem to be equally active when brought in contact with the same serum, hence the amount of opsonins present in the blood of an individual determines, according to the opsonic theory, his susceptibility to bacterial invasion.

TECHNIQUE.

To measure the resistance of the patient to such invasion, or to find out his opsonic index, special technique has been developed, which may be briefly described as follows:

I. EMULSIONS OF BACTERIA.

Twenty-four-hour or younger growths of the rapid-growing bacteria, as Staphylococci, Streptococci, Pneumococci, Gonococci and Colon bacilli, upon inclined agar are washed off with normal saline solution. After the mixture has sedimented, the upper, whitish layer composed of fluid and bacteria is removed with a pipette, and the finer clumps of bacteria precipitated by placing the fluid in a rapidly rotated centrifuge for a few minutes. The supernatant layer, which is still opalescent and is called a bacterial emulsion, should if suitable for work contain the germs in a well-separated condition.

Cultures of tubercle germs are heated, and ground in a mortar with salt solution until the mass is well broken up, and then centrifugated. In case glycerin cultures are used, such as are left in the

manufacture of Koch's old tuberculin, the glycerin must be removed by repeated washing with water and finally with 1.5 per cent, salt solution. The washed culture is worked up in a mortar and centrifugated until the clumps are practically all thrown down, and the cloudy layer or emulsion is removed.

The emulsions must be of uniform density. Wright computed the number of germs in a given volume by counting, but McFarland and L'Engle devised an apparatus which is called a nephelometer, consisting essentially of mixtures of BaSO4, put up in sealed tubes, which correspond to solutions containing from I to IO per cent. of BaCl₂, which serve as standards. The turbidity of the emulsion is compared in similar layer with the standard tubes of BaSO. They found that the tube containing "5 per cent. of BaCl2 corresponds to the most useful bacterial suspension." The permanency of the emulsions varies a good deal. Suspensions of the gonococci should be used at once, staphylococci within two days, etc., while the emulsion of tubercle germs may be employed indefinitely.

II. WASHED WHITE BLOOD-CORPUSCLES.

The finger or lobe of the ear is punctured as in making a blood count, and the blood is allowed to drop directly into normal saline, ·85 per cent. solution, containing about I per cent. sodium citrate; this decalcifies the blood and prevents clotting. The corpuscles are completely precipitated in the centrifuge, and then repeatedly washed with .85 per cent. saline and centrifugated, until all traces of the citrate and serum are removed. After the final precipitation the saline solution is withdrawn, and the thin upper grayish layer of the sediment, the leucocytic cream, consisting for the most part of washed white blood cells, is removed.

III. THE SERUM.

Blood is obtained in the usual way, but is collected in small, bent, glass tubes, which can be readily held in the centrifuge and the serum separated. In obtaining normal serum, care must be exercised in selecting a healthy subject, or, what is better, obtain serum from the mixed blood of several normal persons' "Pool."

IV. STAIN.

With the exception of Malta fever and tubercle bacilli, Leishman's stain, consisting of eosin and methylene-blue, in combination, or Jenner's stain, is employed. Carbol-fuchsin is employed for the tubercle bacilli.

METHOD OF OBTAINING OPSONIC INDEX.

Special capillary pipettes, graduated into equal divisions, are reguired; then by means of a rubber tube or bulb equal quantities of washed corpuscles, bacterial emulsion, and patient's serum are taken up, and all blown out upon a glass slide and thoroughly mixed. The mixture is then drawn up in a small pipette, sealed, and placed in an incubator of the ordinary type, or preferably in an opsonic incubator as proposed by Freeman; it is heated to 37° to 40° C. for fifteen minutes. A similar tube is prepared, except that the normal serum or "Pool" is employed instead of the patient's serum. At the end of fifteen minutes the smears on microscopical slides are made from each tube, fixed, and stained. A good field is selected, one containing many leucocytes, the number of germs counted in the first fifty or hundred observed, and an average per leucocyte determined. If the average in the mixture containing the normal serum is two, we would say that the normal opsonic index is two, and if the mixture containing the patient's blood serum is one per corpuscle, we would say that his index was one-half, etc.

Wright and his pupils, as the result of numerous observations, classify diseases due to bacterial infections:

- (1) "Diseases in which the bacterial process is strictly localized" or "shut off from the lymph and blood circulations." Furunculosis, lupus, tuberculosis, etc., in fact most chronic infections, belong to this class. "In this class the opsonic index of the blood is persistently below normal, owing to the absence of immunizing stimuli."
- (2) "Diseases in which the bacterial process is but loosely shut off, especially from the lymph circulation." In these, usually acute, infections immunizing products from the invading bacteria from time to time get into the circulation, and the opsonic index may be normal or above or below normal. Good examples of this class are tuberculous joints, etc.
- (3) "Diseases in which the bacterial infection is in the blood stream." In this class belong acute infectious diseases, septicemia, endocarditis, Malta fever, etc. In these "the opsonic index is generally below normal."

Wright and Douglas lay down the following general principles for treating cases of bacterial infections:

- (1) "Isolate in pure culture the causative microorganism."
- (2) "Estimate the opsonic power of the patient's blood to this microörganism."
- (3) "If the opsonic index be at or below normal, prepare and standardize a vaccine from this microörganism."
- (4) "Inoculate the patient with this vaccine with appropriate doses and at proper intervals, as shown by a systematic estimation of the opsonic content of the patient's blood."

PREPARATION OF VACCINES.

The vaccines, with the exception of the tubercle vaccine, consist of emulsions of heated cultures of the particular germ producing the Luxuriant cultures of the desired organism are grown upon inclined agar; the growth is then removed with salt solution and a glass rod, and thoroughly emulsified by shaking in a test-tube, in order to get the germs well distributed and the clumps broken up. The number of germs in a given quantity of the emulsion is then determined by comparing the number of germs and red bloodcorpuscles in a mixture of one part emulsion, one part freshly drawn blood, and three parts of normal salt solution. If there are ten times as many germs as blood-corpuscles, the bacterial suspension contains approximately 45,000,000 germs per cubic centimeter. The number of germs present will of course vary with the density of the emulsion. The bacterial suspension is heated at the lowest temperature and for the shortest possible time to kill it. The amount of sterilization will differ with different organisms; 60° C. or less maintained for thirty minutes or less is usually sufficient. Cultures from the vaccine are finally made to insure that it is sterile and safe and some preservative added.

Tubercle Vaccine.—This is the "New Tuberculin Koch," an opalescent fluid, containing the active principle of tuberle bacilli obtained according to the method of Koch.

THERAPEUTIC APPLICATION.

After a proper diagnosis has been made, the patient's opsonic index taken, and the appropriate vaccine prepared, the patient receives his initial injection of several hundred millions more or less of the heated bacteria, and his opsonic index is watched. A short time after the inoculation is made the opsonic index falls lower than

it was previous to the injection. This Wright has named the "negative phase." Sooner or later, from a few hours to several days, the opsonic index rises above the starting-point. This is called the "positive phase." The amount of the opsonins in the blood remains stationary for a variable length of time, and then diminishes. As soon as their diminution is noted, a second injection of the vaccine is given, which is followed by a negative phase, but less pronounced than before. Soon the positive phase comes on, reaching a higher level than previously. Thus the injections are repeated from time to time according to the opsonic index of the patient's blood, and the positive phase gradually attains a higher and higher level, until it may be as high as or considerably higher than that of a normal person. In other words, if the vaccinations are properly given, "never during a negative phase," and as a result the patient's tissues are stimulated to an increased production of the opsonins. phagocytosis is increased, the invading bacteria are disposed of, and the patient recovers from his infection. The proper handling of patients according to this method requires the greatest attention to details of technique for obtaining the opsonic index, preparing the vaccine, and the administration of the proper dose at the proper time.

It is too early to know the ultimate results that may be expected from the use of the vaccines, but from personal observation, conversation with other workers, and numerous reports, most of which are incomplete, it seems reasonable to believe that for localized bacterial infections much may be accomplished. Especially does this seem probable for acne, furunculosis, sycosis, abscesses, and lupus, adenitis, and other similar tubercular infections.

In incipient pulmonary tuberculosis encouraging results have been obtained where minute doses of new tuberculin, $\frac{1}{1000}$ of a milligramme more or less, have been given, which seemingly show that Koch's original observations were well grounded in fact.

Something has been accomplished in those diseases in which the bacterial infection is in the blood stream.

After a careful consideration of the literature of the entire subject I believe we should recognize the new therapy as an experimental procedure of much promise, but until more extended observations have been made the use of the vaccines should not be looked upon as a settled method of treatment.

PHARMACEUTICAL MEETING.

The stated Pharmaceutical Meeting of the Philadelphia College of Pharmacy was held on Tuesday afternoon, February 19th, with M. I. Wilbert, Ph.M., in the chair.

Prof Charles H. La Wall was the first speaker on the program, and presented a paper on "The Food and Drugs Act in its Relation to Public Health." (See p. 107.) The author reviewed conditions leading up to the passage of the United States Food and Drugs Act of June, 1906, and in considering the detailed provisions of the law, paid particular attention to the section on misbranding.

Mr. Thomas H. Potts called attention to a form of deception in which it is made to appear that the serial number placed by manufacturers on packages is a Government guarantee number.

Prof. Henry Kraemer said that there is a need for more workers along this line. He referred to the work which has been done by Dr. Wiley, and said that he deserved great credit not only for his efforts in securing the adoption of the Pure Food and Drugs Act, but also for standing out so many years against the moneyed interests represented by unscrupulous manufacturers.

The subject of drug legislation was brought up and Mr. Wilbert said that pharmacists were making a mistake in not taking an active part in it. He stated that in Vermont the druggists had hesitated in the matter, and that the grocers of that State had succeeded in having a law enacted which may prove inimical to the interests of pharmacists. He then called attention to the bill introduced in the Pennsylvania legislature which is practically that of the Wholesale Grocers' Association, and does not exempt physicians' prescriptions and the preparations of the United States Pharmacopæia and National Formulary in those portions of the bill which relate to labelling. Mr. Wilbert further stated that this bill is being introduced in the legislatures in a number of States, while the bill formulated by the Ladies' Home Fournal has now been introduced by twenty State legislatures. It was also mentioned that a bill drafted by the National Wholesale Druggists' Association is being introduced in some States, and that still another draft is that of the Proprietors' Association.

Mr. Potts spoke of the meeting in Chicago of the representatives of the National Association of Retail Druggists, the National

Wholesale Druggists' Association and the Proprietors' Association, and said that an attempt was made to have a law drafted which would require both physicians and retail druggists to use labels giving details as to the composition of medicines prescribed and dispensed. He then remarked that retail druggists are not opposed to legislation which is fair, but that they are not in favor of hasty legislation, which, as proposed in some instances, would drive retail druggists out of business.

A paper on "Sunday Closing: A Means of Elevating Pharmacy," by Clarence H. Campbell, a local druggist, was read in the absence of the author by George B. Weidemann, P.D. The paper contained the statement that at the recent conventions of the National Association of Retail Druggists held in St. Louis and Atlanta, resolutions were unanimously adopted favoring Sunday closing, and that helpful suggestions had been made as to the ways and means of bringing about this end. The writer was of the opinion that the long hours without proportionate compensation has an influence in keeping young men from taking up pharmacy in the first place, or of pursuing it after qualifying for the work. Mr. Campbell also considered some of the arguments that have already been advanced in some of the previous issues of this JOURNAL as to the necessity of reasonable rest and recreation in broadening the horizon of the pharmacist.

Mr. Thomas H. Potts also presented a communication on the subject of Sunday closing and shorter hours. After considering the need of a more liberal spirit on the part of pharmacists and the necessity for an improvement in the number of hours that the pharmacist is on duty, Mr. Potts said that he fully admitted that the public must be taken into consideration, but maintained that they can be educated, and very readily, to acquiesce in this movement if concerted action be taken by druggists.

Mr. Potts further remarked that in his opinion there is only one possible plan to adopt and that is to agitate this question on every favorable opportunity. He said that since the agitation begun last fall by the Philadelphia College of Pharmacy, a great many retailers have closed their stores on Sunday afternoons, and in conversation with some of them he was informed that they like the plan so well that they could not be induced to return to the old conditions.

R. W. Cuthbert, chairman of the committee appointed by the

college to help forward the shorter-hour movement, reported that he was encouraged by the results that had already been attained.

FLORENCE YAPLE, Secretary pro tem.

PROCTER MONUMENT FUND.

GENEROUS SUBSCRIPTION.

Just as we are going to press Professor Remington informs us that Mr. John Wyeth, a graduate of the Philadelphia College of Pharmacy, of the class of 1854, has, for himself, his firm and his brother, subscribed the sum of \$2,000 to the Procter Monument Fund.

Mr. Wyeth has a warm appreciation of the services of Professor William Procter, not only to the cause of education, but to everything which tended to the advancement of pharmacy, particularly his researches on percolation and fluidextracts. It is confidently hoped that Mr. Wyeth's example will be followed by others who have equally profited by the labors of the Father of American Pharmacy.

THE NEW FOOD AND DRUGS LABORATORY.

The Philadelphia College of Pharmacy is about to erect a new laboratory, designed to give instruction in analytical chemistry, technical microscopy, and other branches of science, especially adapted for students who desire to fit themselves for chemists under the Food and Drugs Act.

The College purchased a property a number of years ago, upon which a school-house had been erected in 1825 for the Aimwell School Association. This historic building will be entirely demolished and a new laboratory erected covering the whole lot, 40×60 feet. Plans are being prepared and it is fully expected that it will be ready for occupancy in the early fall. A roster is being drawn up for the courses for the students in the Food and Drug Laboratory, which will be available shortly.

The College has had in contemplation for a number of years a plan for extending the instruction in this department, and the passage of the Food and Drugs Act has caused such a demand for chemists, that immediate steps have been taken to put the plans in execution.